REMARKS

Status of the Claims

Claims 45 and 54-65 are pending in the application. By this paper, claims 45 and 54-57 are amended without prejudice, and claims 60-65 are canceled. Support for the amendments is found, at least, in the claims as filed. No new matter has been added. Accordingly, Claims 45 and 54-59 are at issue.

Rejection of Claims Under 35 U.S.C. §112, Second Paragraph, Antecedent Basis

The Action rejects the use of "said fragment" in Claims 54-57 as lacking sufficient antecedent basis. Applicants note that the claims have been amended in order to advance prosecution. The rejection is thus believed moot and withdrawal thereof is respectfully requested.

Rejection of Claims Under 35 U.S.C. §112, First Paragraph, Enablement

The Action rejects Claims 45 and 54-65 as lacking enablement. In particular, the Action alleges that enablement is not provided for the full scope of the claims because "when given their broadest reasonable interpretation, the claims read on *in-vivo* treatment" and *in-vitro* data predominates in the specification. *See* Office Action at page 4.

In response, and in light of the Interview conducted May 1, 2008 regarding the present application, Applicants note that the full scope of currently claimed subject matter is enabled for the following reasons. "To be enabling, the specification of a patent must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' . . . . Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *See In re Wright*,

999 F.2d 1557 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. M.P.E.P. § 2164.08 (citing *In re Buchner*, 929 F.2d 1557 (Fed. Cir. 1993)). Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive." *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

Here, the proper test for enablement is whether one of ordinary skill in the art would recognize the correlation between *in-vivo* and *in-vitro* data for this type of technology. Given the art-accepted status of the ELISPOT assay, one of ordinary skill would indeed recognize this correlation. The enzyme-linked immunosorbent spot (ELISPOT) assay is a common method for monitoring immune responses in humans and animals, and was developed by Cecil Czerkinsky in 1983. *See* Czerkinsky C, Nilsson L, Nygren H, Ouchterlony O, Tarkowski A (1983). "A solid-phase enzyme-linked immunospot (ELISPOT) assay for enumeration of specific antibody-secreting cells". *J Immunol Methods* 65 (1-2): 109–21. The ELISPOT assay was developed from the ELISA immunoassay, and was originally used to identify B cells secreting antigen-specific antibodies. Under appropriate conditions the assay allows visualization of the secretory product of individual activated or responding cells. Each spot that develops in the assay represents a single reactive cell. Limits of detection are below 1/100,000, making the assay uniquely useful for monitoring antigen-specific responses in a range of areas of immunology research, including cancer, transplantation, infectious disease, and vaccine development. The assay is especially suited for measuring cytotoxic T lymphocyte (CTL) responses, in large part because it is both reliable and highly sensitive. Thus, the ELISPOT assay provides both qualitative (type of immune protein) and quantitative (number of responding cells) information,

and *in-vitro* data derived therefrom is accepted to correlate well with, and thus be predictive of, corresponding *in-vivo* results.

The specification supplies numerous examples of *in-vitro* data relating to the claimed methods. Indeed, the Examiner recognized this fact in an earlier Office Action. "The specification discloses detection of a CTL response against the peptides of SEQ ID Nos. 245, 297, 298, and 301 in peripheral blood cells from melanoma patients (examples 2 and 3)." Office Action issued July 20, 2007 at 6. For example, Figure 1 depicts T-cell response against the ML-IAP_{280} (QLCPICRAPV) peptide as measured in an ELISPOT in peripheral blood lymphocytes (PBL) from the melanoma patient FM3 (FIG. 1A) or FM72 (FIG. 1B) and in tumor-infiltrating lymphocytes (TIL) from the melanoma patient PM9 (FIG. 1C) or FM72 (FIG. 1D). Similarly, Figure 2 shows T-cell response as measured in ELISPOT against the peptides ML-IAP_{280} (QLCPICRAPV), ML-IAP_{245} (RLQEERTCKV), ML-IAP_{230} (VLEPPGARDV), and ML-IAP_{90} (RLASFYDWPL) in TIL samples from nine patients and in PBL from two patients. Figure 3 shows T-cell response against the ML-$IAP_{245\text{-}253}$ (RLQEERTCK) peptide as measured in an ELISPOT in PBL from 14 melanoma patients. Figure 4 depicts *in-situ* detection of ML-IAP-reactive CTL in primary tumors from two HLA-A2-positive melanoma patients. Figure 5 shows cytolytic capacity of ML-IAP-specific CTL.

The above-referenced data, in addition to further disclosure in Examples 2 through 5, is sufficient to teach those skilled in the art to make and use the full scope of the claimed invention without undue experimentation.

Thus, as was discussed during the Interview conducted May 1, 2008, Applicants have adequately enabled the claimed invention. Withdrawal of the rejection is thus respectfully requested.

Rejection of Claims Under 35 U.S.C. §112, First Paragraph, Written Description

The Action rejects claims 45 and 54-65 as failing to comply with the written description requirement of 35 U.S.C. §112, first paragraph. Specifically, the Action asserts that the claims contain subject matter ("functional equivalents having at least 75% sequence identity to" the peptides identified by the SEQ ID Nos. listed) which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants disagree with the basis for this rejection, but have amended the claims solely in order to place the present case in better condition for allowance. Claim 45 has been amended to remove "and functional equivalents having at least 75% sequence identity thereto." Claims depending from claim 45 that contained "functional equivalents" limitations have also been canceled. Applicants reserve the right to pursue the canceled claim scope in one or more continuing applications.

Applicant believes the rejection of the pending claims as lacking written description support in the specification is rendered moot by these amendments. Withdrawal thereof is respectfully requested.

Conclusion

Applicants submit that the present Application is in condition for allowance and respectfully request the same. If any issues remain, the Examiner is cordially invited to contact Applicants' representative at the number provided below in order to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 19-3140.

Respectfully submitted,

Dated: June 27, 2008 By: 

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